58. (New) A product comprising a support material and a plurality of different nucleic acid molecules, wherein

the nucleic acid molecules are attached to the support material,

the nucleic acid molecules comprise a sequence that is complementary to and specific for an exon or an intron of a gene,

said product comprises at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene,

said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

B'

59. (New) A product comprising a support material and a plurality of different nucleic acid molecules, wherein

the nucleic acid molecules are attached to the support material,

the nucleic acid molecules comprise a sequence that is complementary to and specific for an exon-exon or an exon-intron junction region of a gene or RNA,

said product comprises at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA,

said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said junction region in said sample.

60. (New) The product of claim 58 or 59, wherein said plurality of different nucleic acid molecules is obtained by a method of identifying or cloning differentially spliced nucleic acids, said method comprising:

SUB C3

a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of

different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown; and

b) identifying or cloning, from the hybrids formed in a), a population of nucleic acids comprising an unpaired region, said cloned or identified nucleic acids comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples.

SUB C3 cont.

61. (New) The product of claim 58, wherein said plurality of different nucleic acid molecules comprising a sequence complementary to and specific for an exon or an intron of a gene is obtained by a method comprising:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

B' cont.

(b) synthesizing one or several oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

62. (New) The product of claim 59, wherein said plurality of different nucleic acid molecules comprising a sequence complementary to and specific for a junction region of a gene or RNA is obtained by a method comprising:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

(b) synthesizing one or several oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

63. (New) The product of claim 61 or 62, wherein the identification step (a) is based upon compilation of published sequences or sequence information from databases.

64. (New) The product of claim 60, wherein said plurality of different nucleic acid molecules comprises an autologous nucleic acid library characteristic of alternative forms of splicings occurring between messenger and pre-messenger RNAs of a given physiological condition.

65 (New) The product of claim 58 or 59, wherein the support material is selected from the group consisting of a filter, a membrane and a chip.

66. (New) The product of claim 58 or 59, wherein the nucleic acid molecules comprise cDNA fragments.

B' cont.

67. (New) The product of claim 58 or 59, wherein the nucleic acid molecules comprise single-stranded oligonucleotides.

68. (New) The product of claim 67, wherein the nucleic acid molecules comprise single-stranded oligonucleotides of between 5 and 100 bases in length.

69. (New) The product of claim 58 or 59, wherein the nucleic acid molecules are specific of alternative splicings representative of a cell or tissue in a given pathological condition.

70. (New) The product of claim 69, wherein the nucleic acid molecules are specific of alternative splicings representative of a tumor cell or tissue.

71. (New) The product of claim 69, wherein the nucleic acid molecules are specific of alternative splicings representative of a cell or tissue undergoing apoptosis.

72. (New) A product for evaluating the toxicity of a compound or treatment to a cell, tissue or organism, the product comprising a support material and a plurality of different nucleic acid molecules attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell treated by a reference toxic compound or treatment, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

73. (New) A product for evaluating the toxicity of a compound or treatment to a cell, tissue or organism, the product comprising a support material and a plurality of different nucleic acid molecules attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for exon-exon or exon-intron junction regions of genes or RNAs that are spliced in a cell treated by a reference toxic compound or treatment, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA, and said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said junction regions in said sample.

74. (New) The product of claim 72 or 73, wherein said plurality of different nucleic acid molecules is obtained by a method of identifying or cloning differentially spliced nucleic acids, said method comprising:

a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of

different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown; and

b) identifying or cloning, from the hybrids formed in a), a population of nucleic acids comprising an unpaired region, said cloned or identified nucleic acids comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples.

75. (New) The product of claim 72, wherein said plurality of different nucleic acid molecules comprising a sequence complementary to and specific for an exon or an intron retained or spliced in a cell treated by a reference toxic compound or treatment is obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell treated by a reference toxic compound or treatment and determining the sequence of the spliced domain,

(b) synthesizing one or several oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said toxic condition.

76. (New) The product of claim 73, wherein said plurality of different nucleic acid molecules comprising a sequence complementary to and specific for a junction region of a gene or RNA spliced in a cell treated by a reference toxic compound or treatment is obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell treated by a reference toxic compound or treatment and determining the sequence of the spliced domain,

(b) synthesizing one or several oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said toxic condition.

77 (New) The product of claim 72 or 73, wherein the support material is selected from a filter, a membrane and a chip.

78. (New) The product of claim 72 or 73, wherein the nucleic acid molecules comprise cDNA fragments.

79. (New) The product of claim 72 or 73, wherein the nucleic acid molecules comprise single-stranded oligonucleotides.

80. (New) A product for evaluating the therapeutic efficacy of a compound to a cell, tissue or organism, the product comprising a support material and a plurality of different nucleic acid molecules attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell treated by a reference therapeutic compound, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

81. (New) A product for evaluating the therapeutic efficacy of a compound to a cell, tissue or organism, the product comprising a support material and a plurality of different nucleic acid molecules attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for exon-exon or exon-intron junction regions of genes or RNAs that are spliced in a cell treated by a reference therapeutic compound, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA, and said product allowing, when contacted with a sample containing nucleic acids under condition

SUB C6 cont.

allowing hybridisation to occur, the determination of the presence or absence of said junction regions in said sample.

82. (New) The product of claim 80 or 81, wherein said plurality of different nucleic acid molecules is obtained by a method of identifying or cloning differentially spliced nucleic acids, said method comprising:

a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown; and

b) identifying or cloning, from the hybrids formed in a), a population of nucleic acids comprising an unpaired region, said cloned or identified nucleic acids comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples.

B' cont.

83. (New) The product of claim 80, wherein said plurality of different nucleic acid molecules comprising a sequence complementary to and specific for an exon or an intron retained or spliced in a cell treated by a reference therapeutic compound is obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell treated by a reference therapeutic compound and determining the sequence of the spliced domain,

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(b) synthesizing one or several oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said therapeutic condition.

84. (New) The product of claim 81, wherein said plurality of different nucleic acid molecules comprising a sequence complementary to and specific for a junction region of

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a gene or RNA spliced in a cell treated by a reference therapeutic compound is obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell treated by a reference therapeutic compound and determining the sequence of the spliced domain,

(b) synthesizing one or several oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said therapeutic condition.

85 (New) The product of claim 80 or 81, wherein the support material is selected from the group consisting of a filter, a membrane and a chip.

B' cont.

86. (New) The product of claim 80 or 81, wherein the nucleic acid molecules comprise cDNA fragments.

87. (New) The product of claim 80 or 81, wherein the nucleic acid molecules comprise single-stranded oligonucleotides.

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88. (New) A product for evaluating the responsiveness of a subject to a compound or treatment, the product comprising a support material and a plurality of different nucleic acid molecules attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell from a responsive subject treated by a reference therapeutic compound or treatment, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

89. (New) A product for evaluating the responsiveness of a subject to a compound or treatment, the product comprising a support material and a plurality of different nucleic acid molecules attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for exon-exon or exon-intron junction regions of genes or RNAs that are spliced in a cell from a responsive subject treated by a reference therapeutic compound or treatment, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA, and said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said junction regions in said sample.

90. (New) A product comprising a support material and a plurality of different oligonucleotides specific for alternative exons or introns of a gene, wherein the oligonucleotides are attached to the support material, and wherein the oligonucleotides are prepared by:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

(b) synthesizing one or several oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

91. (New) A product comprising, immobilized on a support material, a nucleic acid library comprising a plurality of nucleic acid molecules, wherein each of said nucleic acid molecules comprises a sequence corresponding to a portion of a gene which is

differentially spliced between two physiological conditions of a cell or tissue, said library being enriched for said nucleic acid molecules.

92. (New) A product comprising, immobilized on a support material, a nucleic acid library comprising a plurality of oligonucleotide pairs, each pair of oligonucleotides comprising a first and a second oligonucleotide, wherein said first and second oligonucleotides of each of said pairs comprise sequences corresponding to differentially spliced forms of a gene, said library being enriched for said pairs.

93. (New) A product comprising, immobilized on a support material, a microorganism library comprising microorganisms transformed by a nucleic library of claim 91.

REMARKS

A clean copy of the pending claims is attached. No new matter is added by the above amendments.

If there are any other charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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